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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,070	06/20/2003	Katherine W. Osteryoung	MSU-08153	5938

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EXAMINER	
KUBELIK, ANNE R.	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,070	OSTERYOUNG ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007 and 16 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 December 2006 has been entered.

2. Claims 23-30 are pending.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Applicant's arguments filed 14 December and 16 March 2007 appear to be identical. Only the page numbers of 16 March 2007 response are referenced below.

Claim Rejections - 35 USC § 112

5. Claims 23-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding SEQ ID NO:2, does not reasonably provide enablement for a vector comprising any nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division, and cells, plants and seeds transformed with it. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 10 August 2006, due

to Applicant's amendment of the claims. Applicant's arguments filed 16 March 2007 have been fully considered but they are not persuasive.

The claims are broadly drawn to a vector comprising any nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division, and cells, plants and seeds transformed with it.

The instant specification, however, only provides guidance for isolation of Ftn2 from *Synechococcus* and identification of putative cyanobacterial homologs (examples 4 and 5), which has 17% identity to an unknown protein (SEQ ID NO:2, encoded by the genomic sequence SEQ ID NO:3 and cDNA SEQ ID NO:1) in *Arabidopsis*; mapping the *arc6* mutation in *Arabidopsis* to show that it and the unknown protein map to chromosome 5 (example 2); rescuing the *arc6* mutation by SEQ ID NO:1 (example 2); analysis of the mutant to show that FtsZ rings and filaments are disrupted (example 2); identification of potential Ftn2 homologues from various database sequences (example 3); isolation of an Ftn2 gene from Synechococcus by transposon mutagenesis (examples 4-5); identification of arc5 (examples 6) and Fzo-like (example 7) genes from *Arabidopsis*. The specification teaches that SEQ ID NO:2 does not have a proper DnaJ domain or a complete myb domain, but appears to have a chloroplast targeting sequence and three putative transmembrane helices (pg 90-91).

The instant specification fails to teach how to make any nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3, wherein the nucleic acid encodes a product that functions in photosynthetic prokaryote or plastid division.

Nucleic acids with 90% identity to the 2406 nucleotide long SEQ ID NO:1 would have 240 nucleotide substitutions relative to SEQ ID NO:1. These nucleic acids thus encompass those that encode proteins with 240 amino acid substitutions relative to the 801 amino acid long SEQ ID NO:2; these proteins would be 70% identical to SEQ ID NO:2. Similarly, nucleic acids with 90% identity to the 3667 nucleotide long SEQ ID NO:3 would have 366 nucleotide substitutions relative to SEQ ID NO:3. These nucleic acids thus encompass those that encode proteins with 366 amino acid substitutions relative to 801 amino acid long SEQ ID NO:2; these proteins would be 54% identical to SEQ ID NO:2.

The instant specification fails to provide sufficient guidance for which 366 amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain photosynthetic prokaryote or plastid division activity of the encoded protein. The specification also fails to provide adequate guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

The guidance in the specification with respect to making amino acid substitutions in SEQ ID NO:2 is as follows: Homologs have Dna-J-like domain missing the central HPD motif, a putative myb domain, a TPR repeat and a leucine zipper, although neither of the latter are in SEQ ID NO:2 (pg 59, line 23, to pg 62, line 2).

Variants include mutants, fragments, fusion proteins and functional equivalents, and changes that result in altered regulatory or enzymatic activity. Includes substitutions, deletions and additions. Conservative amino acid substitutions are suggested as not having a major effect

on the biological activity of the protein, but nonconservative substitutions are contemplated, as are amino acid deletions and insertions. Methods of making include site-directed, random mutagenesis and gene shuffling (pg 55, line 22; to pg 59, line 20).

Lastly, Examples 3 and Fig 3 show putative homologs , which have 15-47% identity to SEQ ID NO:2 (Table 4).

Thus, from the guidance in the specification, it would appear that the vast majority of the amino acids in SEQ ID NO:2 could be substituted with any other amino acid.

Making amino acid substitutions in SEQ ID NO:2 is unpredictable.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1).

Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209,

right column, paragraph 2). Thus, making and analyzing proteins with 366 amino acid substitutions that also have Ftn2 activity would require undue experimentation.

Thus, extensive teachings are required for making nucleic acids encoding Ftn2 proteins with 366 amino acid substitutions relative to SEQ ID NO:2, as encompassed by the claimed nucleic acids. These teachings are not provided for by the specification. The specification also fails to overcome the unpredictability of making large numbers of amino acid substitutions in SEQ DI NO:2 as it provides no working examples of proteins with 366 amino acid substitutions relative to SEQ ID NO:2.

The only assay for FTN2 function is complementation of the arc6 mutation with a nucleic acid encoding SEQ ID NO:2 (example 2). It is not clear that other nucleic acids encoding proteins with 366 amino acid substitutions relative to SEQ ID NO:2 would be able to complement this mutant, given the importance of individual amino acids in portion-protein interactions.

Additionally, even 5 years after the filing of the instant application, the function of Ftn2 is not known (Maple et al, Annals Botany 99:565-579; pg 570, right column, paragraph 2). Also, Arc6 (the instant SEQ ID NO:2) appears to have a very different function in plants than Ftn2 does in prokaryotes (pg 570, right column, paragraph , to pg 571, right column, paragraph 2).

The specification also does not teach how to use plants in which Ftn2 is overexpressed. The phenotype of such plants is not taught; thus one of skill in the art would not know how to use them.

As the specification does not describe the transformation of any plant with nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with an unspecified phenotype.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that in Falkner, those with skill in making poxvirus would have the skill to make the invention in that case; in the instant case, the level of skill in the art has not been defined (response pg 6).

This is not found persuasive. Lazar, Hill and Guo teach the level of skill in the art. Guo in particular teaches that, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with 366 amino acid substitutions that also have Ftn2 activity would require undue experimentation.

Applicant urges that one of skill in the art would have 5-10 years creating recombinant genes in transgenic plants and could screen Ftn2 expression in plants (response pg 7).

This is not found persuasive because this would not provide one of skill in the art the experience required to make 366 amino acid substitutions in SEQ ID NO:2 and still provide a functional protein.

Applicant urges that at the time the application was filed, the art was not concerned with

making predictable changes in proteins; the state of the art was to make both conservative and nonconservative changes and test them by expression in a plant (response pg 7).

This is not found persuasive because making predictable changes what is required to make the claimed nucleic acids.

Applicant urges that one of skill in the art would recognize that there as many possible sequences within the claimed range of 90% homology; the functional limitation has be ignored (response pg 7-8).

This is not found persuasive because the functional limitation does not teach which amino acid substitutions to make. It is not even clear of a functional protein with 366 amino acid substitutions can even be made. Extensive teachings are required for making nucleic acids encoding Ftn2 proteins with 366 amino acid substitutions relative to SEQ ID NO:2, as encompassed by the claimed nucleic acids.

6. Claims 23-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 10 August 2006, as applied to claims 1, 4-6 and 8-17. Applicant's arguments filed 16 March 2007 have been fully considered but they are not persuasive.

The essential feature of the claims is a nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3 and the encodes a product that functions in division of a prokaryote or a

plastid. As the protein and its activity are novel, there is no well-developed field of prior art.

The specification describes FTN2 function as a protein that when its levels are decreased leads to incomplete or no division of a prokaryote or plastid, resulting in long filamentous cells in cyanobacteria and single or few very large chloroplasts in plants (pg 15, lines 1-10).

The specification describes Ftn2 proteins as having a DnaJ-like domain at its N-terminal half, but that this domain is missing the essential central HPD motif (pg 60, lines 7-10; pg 90, lines 12-17). Other motifs are described (pg 60, lines 11-20; pg 90, lines 17-27; Table 7), but such motifs are not present in every protein indicated to be an Ftn2 homolog.

There is no description of the structure required for the recited function, and no description of the necessary and sufficient structural elements of a protein with Ftn2 function.

The only species described in the specification are SEQ ID NOs:3 and 4, which encode SEQ ID NOs:2 and 5, respectively. The putative homologs described in the specification are partial sequences whose function has not been determined.

One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NOs:1, 3 and 4 are insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described a nucleic acid that is at least 90% homologous to SEQ ID NO:1 or 3 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that one of skill in the art would have extensive experience in modifying genes and expressing the modified gene in a plant (response pg 8).

This is not found persuasive because there is no description, in the specification or the art of the structure required for the recited function, and no description of the necessary and sufficient structural elements of a protein with Ftn2 function. Thus, one of skill in the art would not know the structure of the full scope of the claimed nucleic acids, that is of nucleic acids encoding prokaryote or plastid division proteins with 366 amino acid substitutions relative to SEQ ID NO:2.

Applicant urges that the claims specifically recite SEQID NO:1 and 3, all the structure required by law, citing Falkner as stating that macromolecular sequence do not always have to be recited (response pg 8).

This is not found persuasive. Falkner was direct to making a poxvirus that lacks an essential region. Falkner is not drawn to nucleic acids encoding proteins with up to 366 amino acid substitutions relative to the original protein. All the regions essential for Ftn2 function are not known in the art. Further, the claims are not limited to Ftn2 function, but to any function involved with prokaryote or plastid division. The structures of SEQ ID NO:1 and 3 do not describe the structure-function relationship in proteins with up to 366 amino acid substitutions relative to SEQ ID NO:2.

7. Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The rejection is modified from the rejection from the rejection set forth in the Office action mailed 10 August 2006. Applicant's arguments filed 16 March 2007 have been fully considered but they are not persuasive.

It is not clear in claim 29 if the plant seed comprise the vector or of the seed is transgenic because it has been transformed with some other nucleic acid.

Applicant urges that the amendment obviates the rejection (response pg 6).

This is not found persuasive for the reasons above.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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Anne Kubelik, Ph.D.
May 9, 2007

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